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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,397	12/20/2001	George L. Murphy	AMBI:076US	2120

7590 06/26/2003

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EXAMINER	
CHAKRABARTI, ARUN K	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/029,397	Murphy
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 1, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above, claim(s) *55-82* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-46, 48-54, and 83-85* is/are rejected.

7) ☒ Claim(s) *47* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, corresponding to claims 1-54 and 83-85, submitted on January 22, 2003, and election of species SEQ ID NO: 60 and 17, submitted on March 18, 2003 and May 1, 2003 respectively are hereby acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 83-85 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 83 is dependent on non-elected and therefore non-existent claim 55. In absence of claim 55, the breadth of the claims are not clear. The metes and bounds of the claims are vague and indefinite.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997).

Urdea et al teach a method for depleting or isolating a targeted nucleic acid from a sample (Abstract) comprising:

a) incubating the sample with a first bridging oligonucleotide comprising (a) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the first targeting region and the targeted nucleic acid (Figures 1-12 and Examples 1 and 5);

b) incubating the first bridging oligonucleotide with a capture oligonucleotide comprising a nonreacting structure and a capture region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the bridging region and the capture region (Figures 1-12 and Examples 1 and 5 and Claims 1-8); and

c) isolating the targeted nucleic acid from the remainder of the sample (Examples 1-5).

Urdea et al teach a method, wherein the sample comprises both eukaryotic and prokaryotic nucleic acid (Column 5, line 63 to Column 6, line 6 and Column 10, lines 27-45).

Urdea et al teach a method, wherein the bridging region, targeting region, or capture region comprises at least 10-20 nucleic acid residues (Examples 1 and 2).

Urdea et al teach a method further comprising incubating the sample with a second bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues,

under conditions allowing hybridization between the targeting region of the second bridging oligonucleotide and the targeted nucleic acid (Examples 1 and 2).

Urdea et al teach a method, wherein the targeting region of the first bridging oligonucleotide is complementary to the sequence of a targeted nucleic acid and the targeting region of the second bridging oligonucleotide is complementary to a different sequence of a targeted nucleic acid (Examples 1 and 2).

Urdea et al teach a method, wherein the targeting region of the first bridging oligonucleotide and the targeting region of the second bridging oligonucleotide are complementary to the same or different targeted nucleic acid (Examples 3-4)

Urdea et al teach a method, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence at the 3' or 5' end of the targeted nucleic acid (Examples 1 and 2).

Urdea et al teach a method, wherein the first bridging oligonucleotide comprises two bridging regions (Examples 1 and 2).

Urdea et al teach a method, wherein the bridging oligonucleotide or the capture oligonucleotide is DNA (Examples 1 and 2).

Urdea et al teach a method, further comprising washing the capture oligonucleotide after incubation with the sample and the bridging oligonucleotide (Example 2, Column 25, lines 6-7).

Urdea et al teach a method, wherein steps a) and b) are performed at the same temperature and time (Examples 1 and 2).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 19-27, 29-31, and 39 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 100 and 5000 residues or not within 400 residues of the 5' or 3' end of the targeted nucleic acid and wherein the first hybridization (step (a)) and second hybridization (step (b)) are performed at a different temperature.

However, it is *prima facie* obvious that selection of probes to hybridize the specific number of nucleotide residues on a target sequence and a specific selection of temperature to carry out hybridization and linking reaction represent routine optimization with regard to production of a desired length of a nucleic acid polymer, the particular sequence and length of the target nucleic acid to be purified, and desired time to carry out the reaction respectively, which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific selection of probes to hybridize the specific number of nucleotide residues on a target sequence and a specific selection of temperature to carry out hybridization and linking reaction performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

8. Claims 2, 3, 7, 8, and 18 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Hogan et al. (U.S. Patent 6,150,517) (November 21, 2000).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the target nucleic acid is prokaryotic 16S or 23S rRNA or eukaryotic 17S or 18S, or eukaryotic 28S rRNA.

Hogan et al. teaches the method, wherein the target nucleic acid is prokaryotic 16S or 23S rRNA or eukaryotic 17S or 18S, or eukaryotic 28S rRNA (Examples 1-21 and claims 1-140).

Urdea et al does not teach the method, wherein the prokaryotic nucleic acid is from a gram positive or negative bacteria.

Hogan et al. teaches the method, wherein the prokaryotic nucleic acid is from a gram positive or negative bacteria (Examples 1-21 and claims 1-140).

Urdea et al does not teach the method, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA molecule and the targeting region of the second oligonucleotide is complementary to a sequence of the second largest rRNA molecule in the sample.

Hogan et al. teaches the method, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA molecule and the targeting region of the second oligonucleotide is complementary to a sequence of the second largest rRNA molecule in the sample (Examples 1-21).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the target nucleic acid is prokaryotic 16S or 23S rRNA or eukaryotic 17S or 18S, or eukaryotic 28S rRNA of Hogan et al. in the method of nucleic acid isolation of Urdea et al. since Hogan et al. state, "We have discovered and describe herein a novel method and means for designing and constructing DNA

probes for use in detecting unique rRNA sequences in an assay for the detection and/or quantitation of any group of non-viral organisms (Column 2, lines 23-27)". Moreover, further motivation is provided by Urdea et al as Urdea et al states, "New techniques are provided for substantially reducing background signals encountered in solution phase hybridization assays (Abstract, first sentence)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the target nucleic acid is prokaryotic 16S or 23S rRNA or eukaryotic 17S or 18S, or eukaryotic 28S rRNA of Hogan et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Hogan et al., of a discovery which provides method and means for designing and constructing DNA probes for use in detecting unique rRNA sequences in an assay for the detection and/or quantitation of any group of non-viral organisms and also in order to achieve the express advantages, as noted by Urdea et al., of an invention which provides new techniques for substantially reducing background signals encountered in solution phase hybridization assays.

9. Claim 4 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Yokoyama et al. (Gene (2000), Vol. 258, pages 127-139).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the rRNA comprises the sequence having SEQ ID NO: 60

Yokoyama et al. teaches the method, wherein the rRNA comprises the sequence having SEQ ID NO: 60 (Table 1)..

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the rRNA comprises the sequence having SEQ ID NO: 60 of Yokoyama et al. in the method of nucleic acid isolation of Urdea et al. since Yokoyama et al. state, "EHEC causes not only hemorrhagic colitis, but also serious complications such as hemolytic uremic syndrome and thrombotic thrombocytopetic puprpura, sometimes resulting in death (Page 128, Column 1, lines 12-15)". Moreover, further motivation is provided by Urdea et al as Urdea et al states, "New techniques are provided for substantially reducing background signals encountered in solution phase hybridization assays (Abstract, first sentence)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the target nucleic acid is Seq ID NO: 60 of Yokoyama et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Yokoyama et al., of a discovery which provides detection of nucleic acids that causes not only hemorrhagic colitis, but also serious complications such as hemolytic uremic syndrome and thrombotic thrombocytopetic puprpura, sometimes resulting in death and also in order to achieve the express advantages, as noted by Urdea et al., of an invention which provides new techniques for substantially reducing background signals encountered in solution phase hybridization assays.

10. Claim 32 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Lodes et al. (PCT International Publication Number WO 01/77168 A2) (October 18, 2001).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the targeting region of the bridging oligonucleotide comprises SEQ ID NO: 17.

Lodes et al. teaches the method, wherein the targeting region of the bridging oligonucleotide comprises SEQ ID NO: 17 (Page 69, SEQ ID NO: 218).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the targeting region of the bridging oligonucleotide comprises SEQ ID NO: 17 of Lodes et al. in the method of nucleic acid isolation of Urdea et al. since Lodes et al. states, "The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly lung cancer (Abstract, last sentence)". Moreover, further motivation is provided by Urdea et al as Urdea et al states, "New techniques are provided for substantially reducing background signals encountered in solution phase hybridization assays (Abstract, first sentence)". An ordinary practitioner would have been motivated to combine and substitute the method,wherein the targeting region of the bridging oligonucleotide comprises SEQ ID NO: 17 of Lodes et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Lodes et al., of a discovery which provides compositions that are useful, for example, in the diagnosis, prevention

and/or treatment of diseases, particularly lung cancer and also in order to achieve the express advantages, as noted by Urdea et al., of an invention which provides new techniques for substantially reducing background signals encountered in solution phase hybridization assays.

11. Claim 46 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Toback et al. (U.S. Patent 6,482,934 B1) (November 19, 2002).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the hybridizing oligonucleotides are incubated in a buffer comprising TMAC.

Toback et al. teaches the method, wherein the hybridizing oligonucleotides are incubated in a buffer comprising TMAC (Column 20, lines 11-20).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the hybridizing oligonucleotides are incubated in a buffer comprising TMAC of Toback et al. in the method of nucleic acid isolation of Urdea et al. since Toback et al. states, "Screening in a tetramethylammonium chloride (TMAC)-containing buffer is also performed, since hybridization of probes with DNA sequences in TMAC is dependent on temperature alone and relatively independent of the G-C content, reducing background (Column 20, lines 12-17)". Moreover, further motivation is provided by Urdea et al as Urdea et al states, "New techniques are provided for substantially reducing background signals encountered in solution phase hybridization assays

(Abstract, first sentence)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the hybridizing oligonucleotides are incubated in a buffer comprising TMAC of Toback et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Toback et al., of TMAC buffer since hybridization of probes with DNA sequences in TMAC is dependent on temperature alone and relatively independent of the G-C content, reducing background and also in order to achieve the express advantages, as noted by Urdea et al., of an invention which provides new techniques for substantially reducing background signals encountered in solution phase hybridization assays.

12. Claim 48 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Hogan et al. (U.S. Patent 6,150,517) (November 21, 2000) further in view of Missel et al. (U.S. Patent 6,300,069 B1) (October 9, 2001).

Urdea et al in view of Hogan et al. teach the method of claim 2 as described above.

Urdea et al in view of Hogan et al. do not teach the method, wherein cDNA is produced using mRNA in the remainder of the sample.

Missel et al. teaches the method, wherein cDNA is produced using mRNA in the remainder of the sample (Abstract and Example 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein cDNA is produced using mRNA in the remainder of the sample of Missel et al. in the method of nucleic acid isolation of Urdea et al. since Missel et al. states, "The compositions and methods of the present invention

useful to generate, replicate, analyze, quantitate and otherwise manipulate nucleic acid molecules are most useful in coupled or uncoupled RT-PCR procedures (Column 6, lines 14-18)". Moreover, further motivation is provided by Urdea et al as Urdea et al states, "New techniques are provided for substantially reducing background signals encountered in solution phase hybridization assays (Abstract, first sentence)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein cDNA is produced using mRNA in the remainder of the sample of Missel et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Missel et al., of compositions and methods to generate, replicate, analyze, quantitate and otherwise manipulate nucleic acid molecules, which are most useful in coupled or uncoupled RT-PCR procedures and also in order to achieve the express advantages, as noted by Urdea et al., of an invention which provides new techniques for substantially reducing background signals encountered in solution phase hybridization assays.

13. Claims 49-53 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Hogan et al. (U.S. Patent 6,150,517) (November 21, 2000) further in view of Missel et al. (U.S. Patent 6,300,069 B1) (October 9, 2001) further in view of Wolber (U.S. Patent 6,465,183 B2) (October 15, 2002).

Urdea et al in view of Hogan et al. further in view of Missel et al. teach the method of claim 48 as described above.

Urdea et al in view of Hogan et al. further in view of Missel et al. do not teach the method, wherein the cDNA is attached to a solid support to create a nucleic acid array.

Wolber teaches the method, wherein the cDNA is attached to a solid support to create a nucleic acid array (Column 8, lines 14-20 and Figures 1-3 and Example).

Urdea et al in view of Hogan et al. further in view of Missel et al. do not teach the method, wherein the solid support is plastic multiple-well plate.

Wolber teaches the method, wherein the solid support is plastic multiple-well plate (Figures 1-2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the solid support is plastic multiple-well plate of Wolber in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. further in view of Missel et al. since Wolber states, "This invention relates to arrays, particularly biopolymer arrays such as polynucleotide arrays, which are useful in diagnostic, screening, gene expression analysis, and other applications (Column 1, lines 4-7)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the solid support is plastic multiple-well plate of Wolber in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. further in view of Missel et al. in order to achieve the express advantages, as noted by Wolber, of an invention which provides arrays, particularly biopolymer arrays such as polynucleotide arrays, which are useful in diagnostic, screening, gene expression analysis, and other applications.

14. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Vary (U.S. Patent 5,800,984) (September 1, 1998).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the bridging region of the oligonucleotide comprises a poly-purine or poly pyrimidine region.

Vary teaches the method, wherein the bridging region of the oligonucleotide comprises a poly-purine or poly pyrimidine region (Column 2, lines 32-62 and Example 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method,wherein the bridging region of the oligonucleotide comprises a poly-purine region of Vary in the method of nucleic acid isolation of Urdea et al. since Vary states, "The methods of the invention facilitate the rapid, specific, and automated isolation and/or detection of a nucleic acid target sequence (Column 4, lines 56-58)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the bridging region of the oligonucleotide comprises a poly-purine region of Vary in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Vary, of an invention which facilitates the rapid, specific, and automated isolation and/or detection of a nucleic acid target sequence.

15. Claims 41 and 42 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Simpson et al. (U.S. Patent 6,485,625 B1) (November 26, 2001).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead.

Simpson et al. teaches the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead (Column 42, line 64 to Column 43, line 24).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead of Simpson et al. in the method of nucleic acid isolation of Urdea et al. since Simpson et al. states, "The transport of reaction products on magnetic beads also allows for the concurrent separation of reaction products and unreacted reagent mixtures (Column 43, lines 22-24)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead of Simpson et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Simpson et al., of magnetic beads, which allows for the concurrent separation of reaction products and unreacted reagent mixtures.

16. Claim 43 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Griffith et al. (U.S. Patent 6,197,575 B1) (March 6, 2001).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the nonreacting structure is cellulose.

Griffith et al. teaches the method, wherein the nonreacting structure is cellulose (Column 30, line s 22-31 and Column 33, lines 1-34).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method,wherein the nonreacting structure is cellulose of Griffith et al. in the method of nucleic acid isolation of Urdea et al. since Griffith et al. states, "Filter or porous material below microscale tissue may be chosen or constructed so as to bind denatured, single stranded DNA. Nitrocellulose filters can be used in this manner. The captured DNA can then be characterized through hybridization techniques using oligonucleotide probes (Column 33, lines 1-5)". An ordinary practitioner would have been motivated to combine and substitute the method,wherein the nonreacting structure is cellulose of Griffith et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Simpson et al., of nitrocellulose filters , which captures single stranded DNA that can be subsequently characterized through hybridization techniques using oligonucleotide probes.

17. Claims 44-45 are rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Nerenberg et al. (U.S. Patent 6,531,302 B1) (March 1, 2003).

Urdea et al teaches the method of claims 1, 5, 6, 9-11, 14-17, 28, 33-38, and 40 as described above.

Urdea et al does not teach the method, wherein the nonreacting structure is biotin and isolation of targeted nucleic acid comprises incubating the sample with avidin or streptavidin.

Nerenberg et al. teaches the method, wherein the nonreacting structure is biotin and isolation of targeted nucleic acid comprises incubating the sample with avidin or streptavidin. (Column 17, lines 36-58).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the nonreacting structure is biotin and isolation of targeted nucleic acid comprises incubating the sample with avidin or streptavidin. of Nerenberg et al. in the method of nucleic acid isolation of Urdea et al. since Nerenberg et al. states, "Particularly useful labels include biotin detectable by binding to labeled avidin or streptavidin (Column 17, lines 51-53)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the nonreacting structure is biotin and isolation of targeted nucleic acid comprises incubating the sample with avidin or streptavidin. of Nerenberg et al. in the method of nucleic acid isolation of Urdea et al. in order to achieve the express advantages, as noted by Nerenberg et al., of particularly useful labels including biotin detectable by binding to labeled avidin or streptavidin.

18. Claim 54 is rejected under 35 U.S.C. 103(a) as being obvious over Urdea et al. (U.S. Patent 5,681,697) (October 28, 1997) in view of Hogan et al. (U.S. Patent 6,150,517) (November 21, 2000) further in view of Vary (U.S. Patent 5,800,984) (September 1, 1998) further in view of Simpson et al. (U.S. Patent 6,485,625 B1) (November 26, 2001).

Urdea et al. in view of Hogan et al. teach the method for depleting rRNA from a sample as described above as described above.

Urdea et al in view of Hogan et al. do not teach the method, wherein the bridging region of the oligonucleotide comprises a poly-purine region.

Vary teaches the method, wherein the bridging region of the oligonucleotide comprises a poly-purine region (Column 2, lines 32-62 and Example 2).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method,wherein the bridging region of the oligonucleotide comprises a poly-purine region of Vary in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. since Vary states, "The methods of the invention facilitate the rapid, specific, and automated isolation and/or detection of a nucleic acid target sequence (Column 4, lines 56-58)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the bridging region of the oligonucleotide comprises a poly-purine region of Vary in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. in order to achieve the express advantages, as noted by Vary, of an invention which facilitates the rapid, specific, and automated isolation and/or detection of a nucleic acid target sequence.

Urdea et al. in view of Hogan et al. further in view of Vary do not teach the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead.

Simpson et al. teaches the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead (Column 42, line 64 to Column 43, line 24).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time

the invention was made to combine and substitute the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead of Simpson et al. in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. further in view of Vary since Simpson et al. states, "The transport of reaction products on magnetic beads also allows for the concurrent separation of reaction products and unreacted reagent mixtures (Column 43, lines 22-24)". An ordinary practitioner would have been motivated to combine and substitute the method, wherein the samples are incubated with magnetic bead followed by the isolation of the magnetic bead of Simpson et al. in the method of nucleic acid isolation of Urdea et al in view of Hogan et al. further in view of Vary in order to achieve the express advantages, as noted by Simpson et al., of magnetic beads, which allows for the concurrent separation of reaction products and unreacted reagent mixtures

Allowable Subject Matter

19. Claim 47 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

20. Any inquiry concerning this communication or earlier communications from the examiner

should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau, whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti

Patent Examiner

Art Unit 1634

June 5, 2003